REMARKS

Applicant respectfully requests reconsideration. Claims 1-5, 8-11, 17-31, 35-36, 38-41, 47-56, 140, 148-160, 165-166 were previously pending in this application. Claims 161-164 are withdrawn as being directed to a non-elected invention. Claims 1-5, 8-11, 17-31, 35-36, 38-41, 47-56, 140 and 148 are canceled herein. As a result, claims 149-160, 165 and 166 are still pending for examination with claims 149, 157, 165 and 166 being independent claims. No new matter has been added.

Information Disclosure Statement

The Examiner has requested copies of all non-patent references because the parent case (US 6703228) is in interference and the paper record cannot be obtained by the Examiner. Applicant notes that the Interference is complete. Applicant has successfully maintained the patent. Thus, it is believed that the Examiner has access to these files again. However, in order to expedite prosecution, Applicant has enclosed copies of all non-US patents references cited in the IDS in the instant case.

Rejection Under 35 U.S.C. 112

Claims 17-21, 25 and 27 are rejected under 35 U.S.C. §112, second paragraph for indefiniteness.

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 17-21, 25 and 27. Therefore the rejection is now moot.

Accordingly, withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Rejection Under 35 U.S.C. 102

Claims 1-3, 5, 8, 17-27, 38-39, 47-49, 51-52, and 54-55 were rejected under 35 U.S.C. §102(b) as being anticipated by Shuber (US Patent 5589330 December 31, 1996).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 1-3, 5, 8, 17-27, 38-39, 47-49, 51-52, and 54-55. Therefore the rejection is now moot.

Accordingly, withdrawal of the rejection under 35 U.S.C. §102, is respectfully requested.

Rejection Under 35 U.S.C. 103

Claims 4, 36, and 53 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Saiki et al. (WO 89/11548 November 30, 1989).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 4, 36, and 53. Therefore the rejection is now moot.

Claims 9-11, 40, 140 and 148 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Hoffman et al. (American Journal of Medical Genetics 1998 Vol. 80 p. 140).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 9-11, 40, 140 and 148. Therefore the rejection is now moot.

Claims 28-30 and 56 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Drmanac et al. (US Patent 6383742 May 7, 2002).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 28-30 and 56. Therefore the rejection is now moot.

Claims 31 and 35 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Drmanac et al. (US Patent 6383742 May 7, 2002) as applied to Claims 28-30 above and in further view of Manos et al. (US Patent 5182377 January 26, 1993).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claims 31 and 35. Therefore the rejection is now moot.

Claim 41 is rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Hoffman et al. (American Journal of Medical Genetics 1998 Vol. 80 p. 140) as applied to Claims 9-11 and 40 above and further in view of Saiki et al. (WO 89/11548 November 30, 1989).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claim 41. Therefore the rejection is now moot.

Claim 50 is rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996).

Without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has canceled claim 50. Therefore the rejection is now moot.

Claims 149-153 and 155-156 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Saiki et al. (WO 89/11548 November 30, 1989) as applied to Claims 4 and 36 and further in view of Cheung et al. (Proceedings National Academy Science 1996 Vol 93 p. 14676).

According to the Examiner, Shuber teaches a reduced complexity genome (RCG) and methods for detecting the presence or absence of SNP alleles in the native RCG using ASO probes. In addition, according to the Examiner, Saiki teaches a hybridization assay in which oligonucleotides (ASO) probes are attached to a solid support. Further, according to the Examiner, neither Shuber, nor Saiki et al. teaches a method using randomly primed PCR to produce the RCG. Finally, according to the Examiner, Cheung et al. teaches preparing a randomly primed PCR-derived reduced complexity genome with at least one primer.

The teachings of Shuber, Saiki et al., and Cheung et al. would not have produced the current claimed invention in the manner suggested by the Examiner as Shuber does not teach a "reduced complexity genome" (RCG). The Examiner has stated that Shuber provides the teaching of a RCG.

Applicant respectfully traverses. The instant application defines a reduced complexity genome as "a reproducible *fraction* of an isolated genome which is composed of a plurality of DNA fragments" (page 16, line 22). Each fragment of the reduced complexity genome has a common sequence at the end. Independent claim 149 requires that the RCG contains less than 20% of the genomic material present in a whole genome. Shuber describes a composition that is a combination of a target genome (a DNA sample isolated from a patient) and PCR-amplified fragments of specific regions of the target genome. The PCR-amplified fragments are present in the composition in an increased concentration (Column 4, line 10-20, see also Example 1). Additionally each fragment within the material used by Shuber does not have a common sequence. Thus, the genome as described by Shuber is not a "reduced complexity genome", as claimed in the claim 149 and the claims dependent thereon.

Further, even if one skilled in the art combined the teachings of Shuber and Cheung et al in the manner described by the Examiner the combination would not have produced the claimed invention. Cheung et al. teaches a method of DOP-PCR (degenerate oligonucleotide primed PCR). The authors state that "we demonstrate that DOP-PCR can be used for whole genome amplification" (page 14677 last paragraph). The authors continue with "our data suggest that DOP-PCR can be used to achieve several hundred-fold amplification of virtually all sequences in the human genome". Cheung's method is performed under conditions that promote amplification of as much of the genomic DNA as possible. Thus, if one of skill in the art combined the method taught by Cheung et al. with the method taught by Shuber, one would not produce a reduced complexity genome having less than 20% of genomic material present in the whole genome, as claimed in the current invention.

Therefore, the combination of Shuber, Saiki et al., and Cheung et al would not have produced the claimed invention.

Claims 157-159 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Saiki et al. (WO 89/11548 November 30, 1989) and Hoffman et al. (American Journal of Medical Genetics 1998 Vol. 80 p. 140) as applied to

Claims 41 above and further in view of Cheung (Proceedings National Academy Science 1996 Vol 93 p. 14676).

According to the Examiner, Shuber teaches a reduced complexity genome (RCG) and methods for detecting the presence or absence of SNP alleles in the native RCG using ASO probes. In addition, according to the Examiner, Saiki teaches a hybridization assay in which ASO probes are attached to a solid support. Also, according to the Examiner, Hoffman et al. teaches a method of detecting genetic alterations in tumor samples. Further, according to the Examiner, neither Shuber, nor Saiki et al. teaches a method using randomly primed PCR to produce the RCG. Finally, according to the Examiner, Cheung et al. teaches preparing a randomly primed PCR-derived reduced complexity genome with at least one primer.

Applicant respectfully traverses. The combination of Shuber, Saiki et al., Hoffman et al. and Cheung et al. as suggested by the Examiner would not have produced the current claimed invention. Shuber, Saiki et al. and Cheung et al. are discussed above. The combination of Shuber, Saiki et al. and Cheung et al. do not produce a RCG having less than 20% of genomic material present in the whole genome. Independent claim 157 includes the limitation that the RCG contains less than 20% of genomic material present in a whole genome. The teachings of Hoffman pertain to the detection of genetic alterations in tumor samples. Hoffman et al. remains silent on a reduced complexity genome and does not provide the missing teaching. Therefore, the combination of Shuber, Saiki et al., Hoffman et al. and Cheung et al., would not have produced the claimed invention.

Additionally, Hoffman et al. was published on November 2, 1998, after Applicant's priority date of September 25, 1998.

Claims 165 and 166 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Cheung et al. (Proceedings National Academy Science 1996 Vol 93 p. 14676).

According to the Examiner, Shuber teaches a reduced complexity genome (RCG) and methods for detecting the presence or absence of SNP alleles in the native RCG using ASO probes, and hybridizing the RCG with ASO probes to detect allelic associations. Further, according to the Examiner, Shuber does not teach a method using randomly primed PCR to produce the RCG.

Finally, according to the Examiner, Cheung et al. teaches preparing a randomly primed PCR-derived reduced complexity genome with at least one primer.

Applicant respectfully traverses. A combination of Shuber and Cheung et al. would not have resulted in the claimed invention. As discussed above, neither Shuber nor Cheung et al, teach a reduced complexity genome. Therefore, the combination of Shuber, and Cheung et al. would not have rendered the claimed invention obvious.

Claims 149 and 154-156 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Saiki et al. (WO 89/11548 November 30, 1989) as applied to Claims 4, 36, and 53 above and further in view Drmanac et al. (US Patent 6297006 October 2, 2001).

According to the Examiner, Shuber teaches a reduced complexity genome (RCG) and methods for detecting the presence or absence of SNP alleles in the native RCG using ASO probes, and hybridizing the RCG with ASO probes to detect allelic associations. Also, according to the Examiner, Saiki et al. teaches a nucleic acid hybridization probe assay in which oligonucleotide (ASO) probes are attached to a solid support. Further, according to the Examiner, neither Shuber nor Saiki et al. teaches a method using randomly primed PCR to produce the RCG. Finally, according to the Examiner, Drmanac et al. teaches a method for producing RCGs by digesting a gene with restriction enzymes and performing PCR with a small set of DNA adapters.

Applicant respectfully traverses. The teachings of Shuber, Saiki et al., and Drmanac et al. if combined would not have not rendered the claimed invention obvious. Neither Shuber, nor Saiki et al. teaches a reduced complexity genome. Even if combined, Drmanac et al. would not have provided the missing teaching, namely a reduced complexity genome.

The teachings of Drmanac et al. pertain to the sequencing of a limited number of separate genes or genomic fragments (Column 50, lines 47-50). The target nucleic acid to be sequenced is obtained by cloning or in vitro amplification procedures. In one embodiment the method of Drmanac et al. includes excising genes of interest by restriction enzymes and ligating the resulting nucleic acid fragments comprising the genes of interest to adapters and universal primers, which can subsequently be used for PCR. While the method of Drmanac et al. may result in a target nucleic

acid that is less complex than a complete genome, the target nucleic acid described by Drmanac et al. is not a RCG as claimed. The instant application defines a reduced complexity genome (RCG) as "a reproducible *fraction* of an isolated genome which is composed of a plurality of DNA fragments" (page 16, line 22). The target nucleic acid of Drmanac et al. is merely the isolation of a limited number of genes of interest, rather than the creation of a RCG, according to the claimed invention. Drmanac et al. et al. therefore does not provide the missing teaching, namely a reduced complexity genome. Thus, the combination of references did not render the claimed invention obvious.

Further, one of skill in the art would not have combined the teachings of Shuber and Drmanac et al in the manner suggested by the Examiner. The Examiner has cited 2 potential motivations for combining the references. Applicants disagree with both.

1. "The ordinary artisan would have been motivated to modify the method of Shuber et al. and Saiki et al. to produce the RCG fragments using adapter PCR (randomly primed PCR derived RCGs) as taught by Drmanac et al. because Drmanac et al. teaches that by using a small number of adapters a million different fragments may be specifically amplified in identical conditions." (Office Action page 26-27). Shuber teaches that PCR amplification can be used to increase "the concentration of specific DNA sequences within the target DNA sequence population." (Col. 4 lines 15-18). Using PCR to amplify a million different fragments would have been contrary to the stated purpose of Shuber, to selectively increase the concentration of specific sequences.

2. "The ordinary artisan would be motivated to produce RCGs with adapter PCR, because Drmanac et al teaches that DNA differences between several patients can be analyzed and that this approach eliminates the need fro expensive genetic mapping on extensive pedigrees." (Office Action page 27). One of skill in the art would not have been motivated by this teaching in Drmanac et al to combine it with the hybridization method of Shuber, because this combination would raise the complexity issues that Drmanac et al seeks to avoid. The ease of analysis is achieved by Drmanac through sequencing. Drmanac states that the technique is of "special value when there is no such genetic data or material." (Col. 51 lines 22-23). Shuber teaches that the DNA is hybridized to oligonucleotides, "wherein each oligonucleotide comprises a variant of a known sequences in the DNA samples." (Col.. 2 lines 10-13). Thus, one of skill in the art would not have taken the

Drmanac material and put it into the methods of Shuber, which requires knowledge of genetic data for generation of the ASOs used in the hybridization step.

Thus, one of skill in the art would not have been motivated to combine the references as suggested by the examiner.

Claims 157 and 160 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shuber (US Patent 5589330 December 31, 1996) in view of Saiki et al. (WO 89/11548 November 30, 1989) and Hoffman et al. (American Journal of Medical Genetics 1998 Vol. 80 p. 140) as applied to Claims 41 above and further in view Drmanac et al. (US Patent 6297006 October 2, 2001).

According to the Examiner, Shuber teaches a reduced complexity genome (RCG) and methods for detecting the presence or absence of SNP alleles in the native RCG using ASO probes. In addition, according to the Examiner, Saiki teaches a hybridization assay in which ASO probes are attached to a solid support. Also, according to the Examiner, Hoffman et al. teaches a method of detecting genetic alterations in tumor samples. Further, according to the Examiner, neither Shuber, nor Saiki et al. teaches a method using randomly primed PCR to produce the RCG. Finally, according to the Examiner, Drmanac et al. teaches a method teaches a method for producing RCGs by digesting a gene with restriction enzymes and performing a PCR with a small set of DNA adapters.

Applicant respectfully traverses. The teachings of Shuber, Saiki et al., Hoffman et al. and Drmanac et al. if combined do not render the current claimed invention obvious. As discussed above, none of the cited disclosures by Shuber, Saiki et al, Hoffman et al. and Drmanac et al., teaches a reduced complexity genome. Therefore, a combination of Shuber, Saiki et al., Hoffman et al. and Drmanac et al. did not render the claimed invention obvious.

Accordingly, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Double patenting

Claims 1-5, 8-11, 17-31, 35-36, 38-41, 47-56, 148, 165-166 are rejected on the ground of nonstatutory obviousness-type double patenting as being upatentable over claims 1-27 of US patent No. 6703228.

Applicant has canceled claims 1-5, 8-11, 17-31, 35-36, 38-41, 47-56 and 148.

Applicant defers any further rebuttal of this rejection until it is the last remaining rejection. In doing so, Applicant is not conceding the propriety of any of the Examiner's statements with respect to the cited and the present claims. Applicant will consider filing a terminal disclaimer to overcome the nonstatutory obviousness-type double patenting rejection.

Accordingly, withdrawal of the nonstatutory obviousness-type double patenting rejection is respectfully requested.

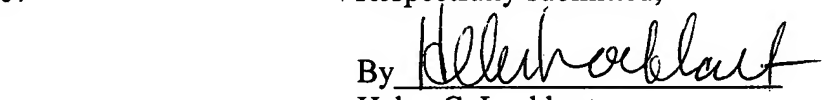
CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: July 30, 2007

Respectfully submitted,

By 

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